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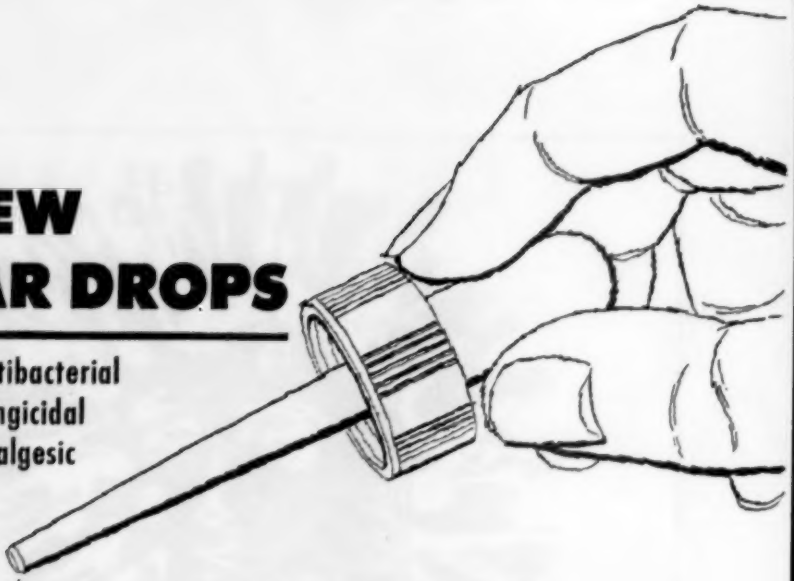

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EDITORIAL

THE CHANGE IN THE A. M. A. CODE OF ETHICS.

PHARMACISTS everywhere are deeply chagrined and even resentful at the recent action of the House of Delegates of the A. M. A. in changing the medical Code of Ethics. After a fairly one-sided debate, a vigorous and well-organized minority pushed through a proposal whereby the operation of a pharmacy by a physician or a group of physicians is not to be considered unethical "provided the patient is not exploited."

Space does not permit a full review of the events leading to this radical departure on the part of organized medicine. Suffice it to say that it was born and nurtured by those who see in modern pharmacy a source of added income. Frequently, today, a prescription for one of our miracle drugs costs the patient more than the physician's fee. This cannot be helped as everyone knows. It was, we suppose, inevitable that this would bring a jealous gleam to the eye of some few physicians who, although dedicated to human welfare, still were very, very human in their traits and weaknesses including greed.

The argument has been advanced that bricklayers and plumbers may own a pharmacy; why not physicians? On the surface this seems good logic, but is it? Bricklayers are not in a position to influence greatly the trend in prescription writing or pharmaceutical service. Pharmacists do not fear such ownership since it poses little in the way of a threat to their profession. By the very nature of the relationship between medicine and pharmacy, the invasion of pharmacy by medicine can be a malignant growth which may eventually throttle the profession in a grip of death. Indeed, pharmacists have as much reason to fear this invasion as medicine fears creeping socialism which in time may threaten the practice of medicine as we know it.

Just as medicine fears the usurpation of its prerogatives by government, we fear the invasion of ours by medicine. The analogy

may indeed not end here for, in ignoring its sister profession and threatening to engulf it, medicine may lose a useful ally in its fight to avoid the octopus of government operation and control.

Who more than pharmacy stood shoulder to shoulder with medicine a few years ago when the forces arrayed in favor of socialized medicine were strong and seemingly invincible? "But," some will say, "that is all over, we won once and for all." Have they indeed? It takes little vision to see that those who believe in socialized medicine are still active and strong. Witness the sentiment in Congress in favor of free poliomyelitis vaccine regardless of ability to pay. What about the scope of the Veterans Administration's medical activities, the Armed Forces, the Public Health Service? Are not labor unions expanding their health services to the point that soon they will clamor for government support or operation?

It would be well for our medical colleagues to see this change in policy on their part as we see it, just as they ask others to look with disfavor upon the invasion of medicine's special province. Pharmacists have a perfect right to be greatly disturbed for it is no small matter. Of course, the change in the Code of Ethics will not overnight convert all physicians to dispensing doctors but it is from such small beginnings that great revolutions grow.

The medical profession can ignore our objections and displeasure —that is their privilege. We can in desperation adopt all sorts of counter-measures, some rather nasty to contemplate. Would it not, however, be unfortunate if some future medical historian in studying the events leading to the loss of private enterprise and initiative in medicine concluded that it was the unhealed breach between pharmacy and medicine in 1955 which led to the engulfment of both by a stronger force? Divide and conquer is an old and trite expression but it still works when there are those so self-centered and smug as to believe themselves an exception to the rule. Medicine and pharmacy if they are wise will avoid such contention and ultimate risk. Medicine does not need to practice pharmacy in order to both function and prosper. Greed and avarice plants the seed of its own destruction, and he who lives by the sword will most certainly die by it.

L. F. Tice

BIOLOGICAL INVESTIGATIONS OF POLYMNIA UVEDALIA LINN.

By Sunil C. Datta * and Marin S. Dunn **

OUR interest in the investigation of Polymnia uvedalia Linn. resulted from a recent report about the efficacious use of the plant by the laity in acute arthritic conditions (12). A perusal of literature showed that the American Dispensatory of 1891 (11) contained an account of this plant which had been highly spoken of as a remedy for rheumatism, several years before under the name "bears foot". The tincture of the plant was considered to be useful in splenic enlargement from malarial influence, chronic gastritis, chronic hepatitic enlargement and in hypertrophy of the cervix uteri; its use was suggested in conditions of full flabby sallow tissues, impaired circulation, atonic impairment of function and glandular enlargement. The ointment of the plant was reported to be beneficial as local application in mammary and other glandular tumors or abscesses, in splenic enlargement and in other painful swellings and local inflammations and the efficacy of the drug was considered to be augmented when a tincture was taken internally together with its external use as an ointment (11).

A survey of the literature showed that there is a paucity of information on pharmacognostic characteristics, organogenesis, microchemistry, chemistry and pharmacology of the plant and this paper presents results of investigations along the above lines.

Materials and Methods

Fresh plant materials were obtained from two natural stands, viz., (i) North Carolina, near Greensboro and (ii) Reading, Pennsylvania. Plants were raised from rootstocks, during 1954-'55 in the

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greenhouse and Kilmer botanic garden of the Philadelphia College of Pharmacy and Science. Materials from both sources were used in our investigation.

Studies on pharmacognostic characteristics were made with fresh plant specimens as well as powdered samples of different plant parts. For observing macroscopical features, a hand lens or a simple dissecting microscope was used. The microscopical characteristics were studied with the compound microscope in both hand and microtome sections, which were permanently stained by the use of safranin O and fast green FCF or stained in eosin or safranin O and mounted in glycerin. Microscopic measurements were made with the aid of stage and ocular micrometers and drawings were done with the help of the camera lucida. For quantitative micro-analytical measurements such as vein-islet numbers, palisade ratios and stomatal indices, portions of leaves were cleared in chloral hydrate and mounted in Berlese mountant of the following composition:—distilled water, 10 gms.; dextrose, 5 gms; gum acacia, 8 gms; chloral hydrate 74 gms; glacial acetic acid, 3 gms.

For determining vein-islet numbers, palisade ratios and stomatal indices, the procedures described by Trease (17) were followed.

Microchemical tests were performed with strictly fresh plant materials. Sections of about 60-70 microns thickness were used for these tests, which were carried out according to the procedures described by Johansen (8) for cell wall and cell contents.

Organogenesis was studied from transverse and longitudinal sections prepared by the paraffin method, cut at 8-10 u, and stained in safranin O and fast green FCF (8). Tissues macerated in chromic acid of different strengths (1-5%), washed in water, stained in eosin or safranin O were also studied. For studies of microsporogenesis, young anthers from buds were smeared on slides, fixed in Navashin's fluid and stained according to Johansen's methyl-violet method (8).

Experiments were performed to discover if the ovaries of the disc flowers could be stimulated to grow, by the application of 3-indolepropionic acid on the stigmas of the flowers, but the result was negative. In order to find out whether the ovaries of the ray flowers developed with or without fertilization, young unopened buds were opened and the styles and stigmas of the ray flowers were cut off with fine scissors and the wounds were blocked with paraffin-petroleum jelly. This prevented chances of fertilization and the whole inflores-

cence was allowed to develop without further manipulation under the cover of a paper bag. The result noted was apomictic development of fruits.

Chemical studies consisted of preparing extracts from fresh roots of the plant according to the method described in the National Formulary (16). The roots were carefully washed to get rid of all soil particles, dried to remove external water, weighed, cut into fine pieces and converted into a fine pulp by means of a Waring blendor, with the addition of a little solvent used for extraction. The material was then transferred to a cylindrical type of percolator and packed firmly; 60% or 95% ethyl alcohol was used as the solvent and it was added on top of the material and the drug was allowed to macerate for 24 hours. The percolation was then allowed to proceed slowly and sufficient solvent was gradually added to the percolator to produce the desired volume of extract. The proportion of alcohol, in each case, was adjusted in such a way that each 100 ml. of the extract contained materials from 20 gms. of fresh roots.

A few preliminary investigations were undertaken for the presence of carbohydrates, tannins and resin, according to the methods described by Rosenthaler (14) in order to determine qualitatively the nature of constituents in the root.

Preliminary pharmacological activity was tested with the alcoholic extract of the roots. It was evaporated to a solid resinous residue under vacuum, then made into an emulsion with distilled water, the amount of water being added in such a way that 1 ml. of emulsion was equivalent to 2 gms. of fresh drug.

For testing its probability of effectiveness as a remedy for arthritic diseases, the hyaluronidase inhibitor test was performed in vivo and in vitro. These tests depend upon the suggestion (1) that the inflammatory processes are associated with the hyaluronidase imbalance and that the beneficial effects of substances like cortisone are

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Plate I. (1) photograph of plant, × 1/15.
(2) photograph of tuberous roots, × 1/2.
(3) l.s. mature ovule of ray floret, showing the basal portion.
(4) l.s. root apex.
A, dermatogen; B, periblem; C, plerome; D, apical meristem; E, calyptrogen; F, cells of root cap; G, embryo sac.

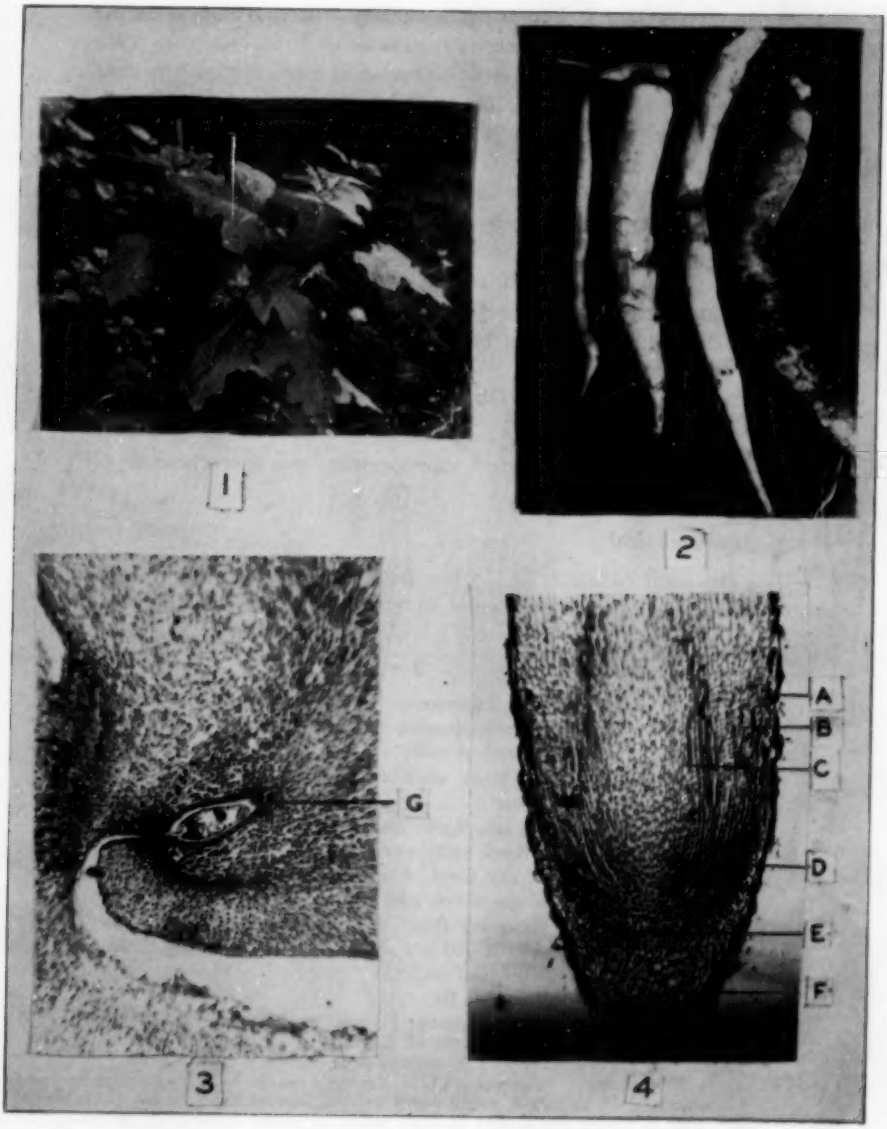

PLATE I

due to their ability to inhibit hyaluronidase. In vivo tests were performed by use of intracutaneous injections of India ink, and noting the spreading area when injected alone, or in a mixture of hyaluronidase and India ink, or in a mixture of India ink, hyaluronidase and plant extract. These tests were performed with 2 rabbits and 3 guinea pigs.

The in vitro tests were done according to a modification of the method of Seastone (15), by using the turbidimetric method and determining the turbidity of mixtures of (i) hyaluronic acid and serum protein, (ii) hyaluronic acid, serum protein, hyaluronidase and aqueous plant extract, by the use of a Beckman DU spectrophotometer with a slit width of 0.07 mm. and a 1 cm. cell.

Observations

Studies on pharmacognostic characters were considered under three heads, viz., macroscopical, microscopical and microchemical and the results are given below.

A. *Macroscopical*

The plant (Plate I, fig. 1) is a large perennial attaining a height of about 2 metres and is found in rocky situations generally near

---

Plate II. (1) three heads of inflorescence from a terminal branch, × 3/2.
(2) involucre of bracts showing two whorls, × 3/2.
(3) ray flower with bracteole × 6.
(4) l.s. developing floral apex, diagrammatic.
(5) stamen.
(6) l.s. developing disc floret, diagrammatic.
(7) mature disc floret, split open.
(8) t.s. ovary of ray floret, diagrammatic.
(9) l.s. ovary of ray floret, with mature ovule, diagrammatic.
(10) l.s. very young ray floret, diagrammatic.
(11) pollen grains, × 200 and section of a pollen grain, × 400.
(12) l.s. young fruit and seed.
(13) l.s. mature fruit.

A, ovary; B, bract; C, filament; D, corolla of disc floret; E, stamen; F, stigma of disc floret; G, ovule of disc floret; H, ovary of disc floret; I, ovule of ray floret in t.s.; J. embryo-sac; K, outer wall of ovary; L, ovule of ray floret (anatropous); M, embryo sac in l.s.; N, micropyle; O, funiculus; P, corolla in young ray floret,; Q, stigma in young ray floret; R, ovule in young ray floret; S, fruit wall; T, young developing embryo; U, lignified fruit wall; V, mature embryo; W, apical tip of embryo.

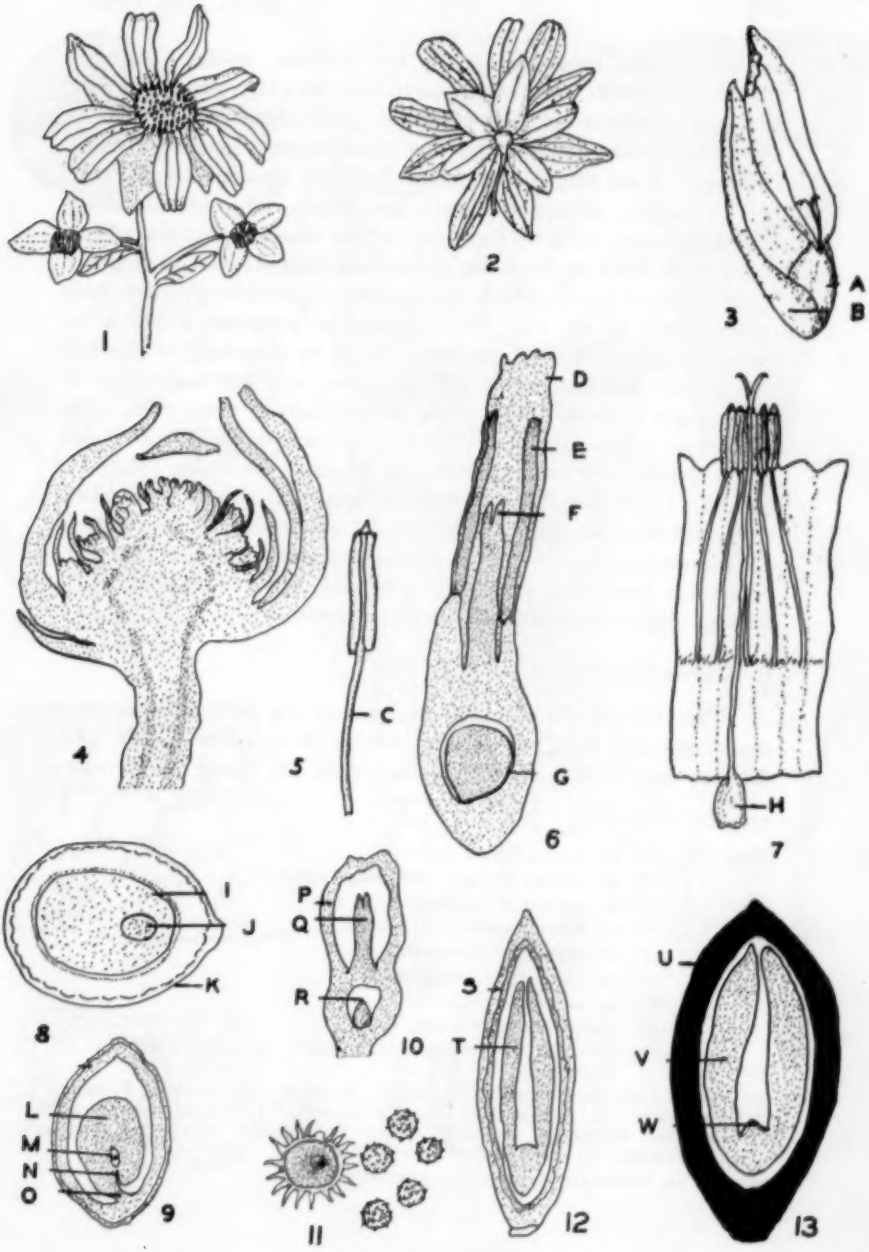

PLATE II

ravines. Roots (plate I, fig. 2) are tuberous, swollen, fusiform, smooth when fresh, longitudinally wrinkled when dry, greyish in color in young condition but dark brown in older ones, with acrid taste, characteristic odor and short fracture which becomes somewhat fibrous and tough in old thin roots. Stems are erect, six-angled (plate III, fig. 4), roughly pubescent. Leaves are simple, sub-palmately lobed, with acute apex, abruptly contracted at the base to short dilated leaf stalks, more hairy on the lower surface and with subpaimate venation. Flowers are in heads, which are arranged in moderately open leafy cymes (plate II, fig. 1). The inflorescence possesses a double involucre (plate II, fig. 2), the outer phyllaries consisting of about 5, obtuse-ovate leaf-like scales and the inner ones are lance-ovate to ovate, much broader and generally larger than the outer ones. The ray florets (plate II, fig. 3), are 9 to 10 in number, female, with yellow corolla and are subtended by greenish bracteoles (plate II, fig. 3B). The disc florets (plate II, fig. 7) are many in number, hermaphrodite, regular, perfect, but do not produce fruits, with 5, epipetalous stamens containing spiny pollen grains (plate II, fig. 11). Fruits are formed by ray florets only and they are obovoid, black achenes, slightly flattened and ribbed lengthwise.

B. *Microscopical*

The roots at the apical region possess the same microscopical structure (plate I, fig. 4), as that of other dicotyledonous roots (4). A transverse section made near the tip of the young lateral roots

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Plate III. (1) t.s. young lateral root.
(2) t.s. mature storage root, diagrammatic.
(3) t.s. portion of mature storage root.
(4) t.s. mature stem, diagrammatic.
(5) t.s. portion of young stem.
(6) l.s. shoot apex, diagrammatic.
(7) t.s. portion of leaf.
(8) resin-ducts from roots, in t.s.
(9) glandular and non-glandular hairs from stem, leaf and inflorescence.

A, resin-duct; B, cork; C, cortex; D, xylem; E, cambium; F, vascular bundle; G, hollow pith; H, pith of roots; I, sclerechyma; J, leaf buttress; K, upper epidermal cells; L, palisade cells; M, spongy parenchyma; N, lower epidermal cells.

t.s, transverse section; l.s., longitudinal section.

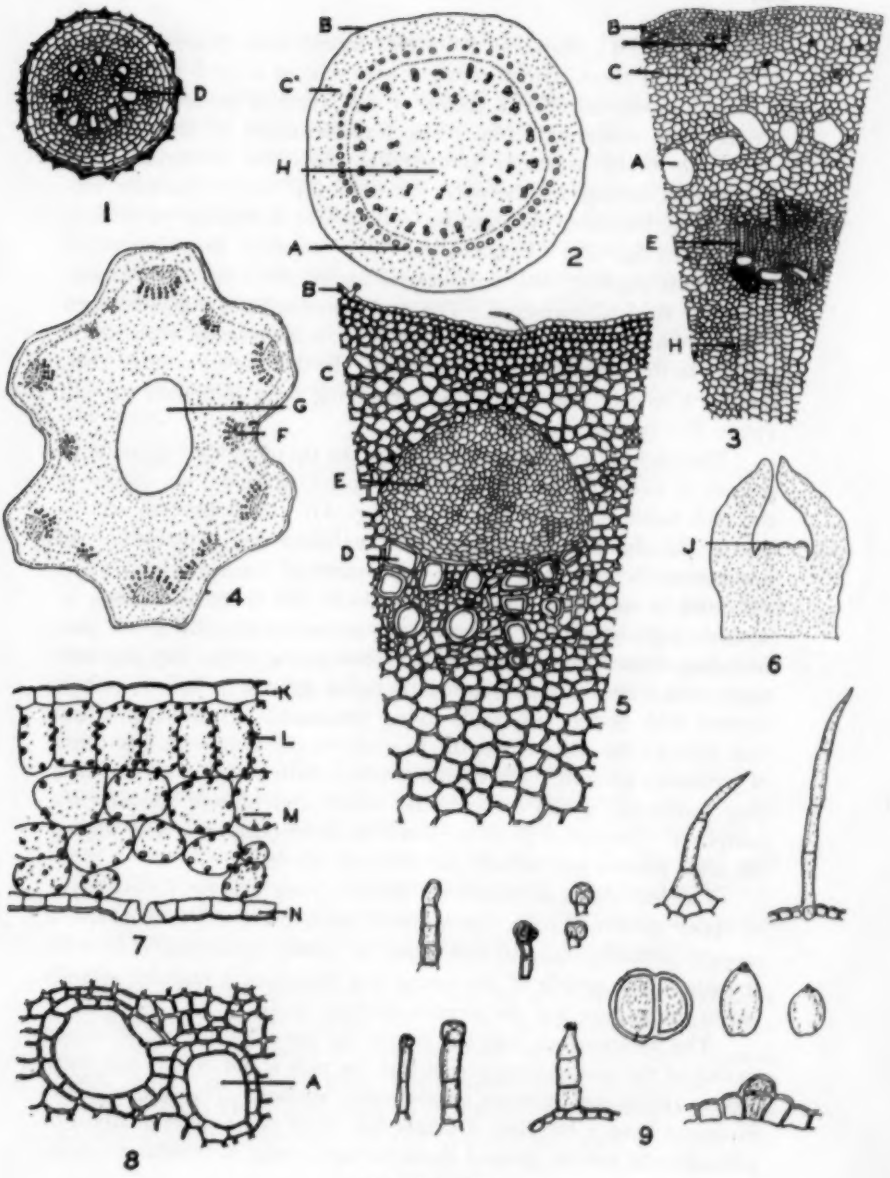

PLATE III

(plate III, fig. 1) shows an 8-10 arch xylem, with phloem strands lying between these xylem archs, a pericycle of 2 to 3 layers, one layer of endodermal cells, a cortex of 4-5 layers of parenchyma and one layer of epidermal cells. The transformation of these young roots into fleshy tuberous roots takes place by proliferation of parenchyma among and between the normally located vascular elements, thus breaking the vascular system into a number of strands (plate III, fig. 2). Hence there is a massive development of parenchyma together with a differentiation of additional vascular elements in this parenchyma. The parenchymatous greatly-enlarged cortex shows in its inner part, a row of schizogenous resin ducts parallel to the boundary of the pericycle. In the mature storage root, there is a ring of collateral bundles resulting from secondary growth (plate III, figs. 2, 3).

The stem, in young stage, *i.e.*, near the tip or at the beginning of growth is found to be solid but as the plant develops, the region of the pith becomes hollow (plate III, fig. 4). In transverse section (plate III, fig. 5), the young stem exhibits the structure of an herbaceous dicotyledon (4). In older parts of the stem, the plan of structure is essentially the same but shows the changes imposed by secondary growth. The pith cells mature very early and as the surrounding tissues go on developing in the young stem, they are torn apart and with the continuation of radial growth a hollow pith is formed with broken cell walls lining the cavity. A transverse section through the old stem at the base of the plant shows a great deal of secondary growth. The cambium strips unite to form a continuous ring producing xylem towards the centre and phloem towards the periphery. Groups of fibers are found to develop more or less capping the sieve masses and phloem parenchyma regions.

The leaf shows in transverse section (plate III, fig. 7) one layer of upper epidermal cells, one layer of palisade cells, 3 to 4 layers of spongy parenchyma, and one layer of lower epidermal cells with stomata. The petiole of the young leaf possesses 3 vascular strands but in the mature leaf the strands increase to 12.

The inflorescence axis has nearly the same histological structure as that of the young stem except that the pith is not hollow and there are no ridges and furrows on the outer surface. The bracts of the involucre have a leaf-like structure but there is no differentiation of palisade cells and the ground tissue contains many intercellular spaces.

The bracteoles possess the same structure as the bracts of the involucre.

The disc florets possess a tubular corolla which in transverse section consists of 2 layers of parenchymatous cells. The anthers show the same structure as those of other dicotyledons (4). The corolla of the ray florets possess a papillate epidermis and the ovary contains one chamber with a single anatropous ovule (plate II, fig. 9). The stigmas of both florets possess an abundance of papillose hairs.

The mature fruit wall (plate II, fig. 13) consists of several layers of sclerenchymatous cells with lignified walls. The embryo with the fleshy parenchymatous cotyledons occupies the interior of the fruit. Two layers of parenchymatous cells lying between the embryo and the fruit wall, mark the position of the remains of the integuments of the ovule.

Powdered drug—(dimensions of cells are the average of 20 determinations).

Root—Dirty greyish in color, and shows the following histological elements: (i) numerous parenchyma cells with reducing sugars, about 25-40μ in diameter, (ii) resin-ducts, up to 200μ long and about 150μ in diameter, (iii) fragments of wood fibers, phloem parenchyma, and other parenchyma cells containing resin masses, (iv) xylem vessels up to 450μ long and about 30μ in diameter and (v) pith cells, up to 90μ in diameter.

Stem—Greyish brown in color with an abundance of glandular and non-glandular hairs, similar to those described under leaf, and are up to 150μ long in case of glandular ones and up to 1000μ long in case of non-glandular ones; collenchyma cells up to 50μ long and about 24μ in diameter, parenchyma cells up to 120μ long and about 45μ in diameter, some with resinous contents; fragments of trachea, wood fibers and bast fibers, wood parenchyma and sieve tubes.

Leaf—Greyish brown in color with an abundance of glandular and non-glandular hairs (plate III, fig. 9), as mentioned under stem. The non-glandular hairs are multicellular, uniseriate with pointed apex, consisting of 5-10 cells, mostly observed as fragments. The glandular hairs are of two kinds: (i) *colleter-type*, with multicellular stalk and multicellular head or (ii) *peltate-type*, with bi-, tetra-, or

multicellular head (5). Other characters are fragments of upper and lower epidermis showing wavy cells and presence of stomata in lower epidermis; palisade cells up to 60μ long and about 30μ in diameter with resin contents; spongy cells, about 60μ x 40μ with resin contents; fragments of trachea, phloem and xylem parenchyma, collenchyma cells from the petiole, up to 180μ long and about 40μ in diameter; parenchyma cells of petiole up to 250μ long and about 120μ in diameter.

Inflorescence—Yellowish to greyish brown in color and shows numerous spheroidal spinose pollen grains, about 25μ in diameter; numerous glandular and non-glandular hairs from the bracts and bracteoles, similar to those described under leaf; parenchyma cells from bracts up to 100μ in diameter; collenchyma from inflorescence axis, up to 120μ long and about 25μ in diameter; papillose epidermal cells of corolla about 120μ x 30μ; parenchyma cells from ovary wall about 30μ in diameter; lignified sclerenchyma from fruit wall, about 50μ x 30μ; fragments of trachea, wood fibers, parenchyma cells, resin-ducts, and phloem fibers.

Microchemical

TABLE I. STUDIES ON CELL WALL AND CELL-CONTENTS.

Tests	*Observations*
i) Sections treated with freshly-prepared chlor-zinc-iodide (Anhydrous zinc chloride, 24 gm.; Potassium iodide, 8 gm.; distilled water 8.5 ml.; Iodine to saturation).	Cells of parenchyma of root and stem, palisade and spongy cells of leaf, and parenchyma of bracts and inflorescence, showed bluish-violet color for cellulose.
ii) Iodine and sulfuric acid (75%).	Showed positive blue reaction of cellulose in the walls of cells mentioned under (i).
iii) Phloroglucinol and hydrochloric acid solution (Phloroglucinol, 1 gm.; ethyl alcohol, 95%, 50 ml.; hydrochloric acid, 40 ml.).	Formation of cherry-red color showed the presence of lignin in cell walls of xylem in root, stem, leaf and inflorescence and in lignified sclerenchyma of fruit wall.

Tests	*Observations*
iv) Chromic acid, aqueous, 50%.	Dissolved all cell walls except cork cells of root and stem and outer walls of epidermal cells of leaf, stem and bracts which contained suberin and cutin, respectively.
v) Potassium hydroxide (conc.) and chlor-zinc-iodide, freshly made.	On boiling the sections in conc. potassium hydroxide, granulated masses of potassium phellonate appeared in cork cells of root and stem, which when cooled, washed with water and treated with chlor-zinc-iodide produced a red-violet color.
vi) Sudan IV (equal parts of a saturated solution of Sudan IV in 95% ethyl alcohol and glycerin).	Showed orange-red color for cutin and suberin in walls of cork cells of root and stem and outer walls of epidermal cells of leaf, stem and bracts.
vii) Ferric chloride solution (1%) aqueous.	Presence of tannin was indicated in parenchyma cells of roots which turned greenish black.
viii) Osazone test: A. (Phenylhydrazine hydrochloride and glycerine, 1:1). B. (Sodium acetate and glycerine, 1:10).	One drop of solution A was mixed with two drops of solution B, then the section was placed in it and slightly heated, when osazone crystals were formed in parenchyma cells of root, showing the presence of reducing sugars.
ix) Fehling's solution.	Sections of root when heated slightly in this solution formed reddish-brown precipitate, showing the presence of reducing sugars in parenchyma cells.

Tests	*Observations*
x) 70% ethyl alcohol.	Inulin crystals were formed in parenchyma cells of the root when sections were kept in alcohol for several days. When tested with thymol and sulfuric acid, they turned red and passed into solution.
xi) Cupric acetate, aqueous, 7%.	Greenish resinous masses were formed in many parenchyma cells of root, stem, leaf, inflorescence, many hairs and resin-ducts after a period of 1-6 days.

Micro-analytical Studies

Quantitative microscopical studies were done with the leaves and determinations were made on (i) vein-islet number, (ii) palisade ratios and (iii) stomatal index.

The vein-islet number which is described (17) as the number of vein-islets per sq. mm. of leaf surface was calculated from 4 contiguous squares in the central part of the lamina, midway between the midrib and margin. During counting, those vein-islets which were not completely within the lines of the counted area were excluded from the count, if cut by the top and left-hand sides of the demarked square area, but were included if cut by the other 2 sides. For determining the average, 5 adult leaves from 3 plants were taken and 4 replicate readings from each leaf in different positions of the same location were considered. The final result was thus calculated from 60 determinations. The range of vein-islet number was found to be from 4.0 to 6.0 with a grand average of 5.2.

The palisade ratio, i.e., the number of palisade cells under 1 epidermal cell was determined from 5 leaves of different sizes, and from each of these, 4 pieces, one from base, apex, centre and margin at the middle part of the lamina, midway between the midrib and margin were taken. Of each section, 3 counts were made and the average value for each leaf was calculated from 60 determinations. The range of palisade ratio was found to be from 6.25 to 7.75 with a grand average of 6.9.

Stomatal index, i.e., the percentage proportion of epidermal cells which has been converted into stomata, was calculated from the formula, $I = \frac{S}{E\text{-}S} \times 100$, where S is the number of stomata per sq. mm. and E is the number of epidermal cells per sq. mm. of leaf surface. Determinations were made on the lower epidermis of the leaf in a position equidistant between the apex and base and between the margin and midrib of each leaf. During the count 2 guard cells were taken as one unit, each hair as 1 unit and each epidermal cell as 1 unit. The area of the field of the microscope under 95 × objective and 10 × ocular, was determined with the aid of stage micrometer and the number of epidermal cells, hairs and stomata present in this field was counted. During counting, those cells which were cut by the boundary line of the upper half of the field were not taken into consideration whereas all the cells present in the lower half of the field were counted as 1 unit each. Determinations were made in 5 different positions of each leaf, all in the same general location and 10 leaves of different sizes were taken into consideration. The final range, calculated from 50 determinations was found to be 14.2 to 17.3 with a grand average of 15.4.

Organogenesis

It was found that the development of the roots, stems and leaves follows the same pattern as described in the case of other dicotyledonous plants (4). Lateral roots were found to arise endogenously from the pericycle just beneath the endodermis, agreeing in development with those described by Esau (4). The cortex of tuberous roots showed the presence of sclerenchyma cells which were not observed in very young roots (plate III, fig. 3, I). The vegetative apex of stem is characterized by 2 layers of corpus and 3 layers of tunica although the boundary is not very prominent. Vacuolation is found to commence in the fifth or sixth cell layer in the central groups of cells derived from the corpus. The increase in the volume of the apex of the stem is brought about by constant division and enlargement of the cells.

The development of the leaf agrees substantially with the pattern of development of other dicotyledonous leaves as described by Esau (4). Axillary buds give rise to branches which show organization of

tissues similar to that of the vegetative stem apex. The bud is initiated by a combination of anticlinal divisions in one or more of the superfical layers of the young axis, and by various divisions in the deeper layers. The change from vegetative to flowering apex is very noticeable as the floral apex becomes flatter and wider and the characteristic activity of the corpus is discontinued as the axis elongation comes to a stop. Further development is associated with the enlargement and vacuolation of cells of the central tissue, and the restriction of the meristematic activity to the peripheral zone for production of floral organs only. The floral organs appear in close sequence on the receptacle as the axis does not elongate any more.

The individual flowers are found to arise acropetally on the flattened receptacle (plate II, fig. 4), so that the outermost flowers are the oldest, the innermost the youngest. The outermost whorl of flowers develop into ray florets while the remaining develop into disc florets. The development of the flowers agrees essentially with that described by Esau (4) for other flowers of Compositae. Microsporogenesis takes place in the normal way with the formation of the dyad and tetrad stage and the four nuclei are walled off simultaneously at the end of meiosis. Later each microspore forms its own wall, consisting of two layers, the exine and intine, the outer wall developing spinous projections.

Megasporogenesis in the disc florets were not studied as the ovaries remained in the rudimentary stage throughout their life. In case of ray florets our observations seem to indicate the presence of many signs of apomixis, such as (i) the formation of tetrads in very young ovules and their subsequent degeneration, (ii) the absence of pollen tube and indication of fertilization, (iii) the presence of embryo-sac with highly vacuolated contents and resting nucleus, (iv) the absence of mitotic division figures, as evidence of apomixis according to the views of a number of workers (2, 3, 7, 9, 10, 13).

It is reported (6) that apomicts are often unable to produce seeds, or their seeds do not reach maturity or do not find suitable conditions of germination and the plant usually propagates itself by vegetative means. Our observations on this plant showed that the plant propagates vegetatively and we were unable to germinate the seeds formed by the ray florets.

The development of the embryo lacks uniformity as in the case of apomictic plants (3), and various stages of degeneration in many

ovules were observed. The endosperm appears as a thin highly vacuolated tissue and is used up completely by the developing embryo which in mature condition contains two large fleshy cotyledons which almost fill the cavity of the fruit. The integument of the ovule with its characteristic innermost layer, the tapetum, (plate I, fig. 3) is crushed during the development of the embryo and its remnant consisting of one or two layers of cells are found in the fully mature seed. The development of the fruit is associated with lignification and thickening of layers of cells of the fruit wall.

Preliminary Chemical Investigations

Chemical investigations on the roots of the plant showed that they contain some reducing sugars, tannin and resin as the chief constituents.

Preliminary Pharmacological Investigations

The in vivo tests showed that when India ink was injected intracutaneously in rabbits and guinea pigs, it remained confined to a spot and did not spread, but when it was mixed with hyaluronidase, it spread out over a large area in the form of pseudopodia as hyaluronidase split hyaluronic acid, a mucopolysaccharide component of intercellular binding cement of connective tissues in the body. When a mixture of hyaluronidase, India ink and the extract of the plant were mixed together and injected intracutaneously, there was little or no spread, thus indicating the property of the extract to inhibit hyaluronidase action. In the case of guinea pigs, the extract of the plant was also injected intraperitoneally and after half an hour a mixture of India ink and hyaluronidase was injected intracutaneously. Spread did not occur, thus suggesting that the extract of the plant acts as a hyaluronidase inhibitor, even when injected intraperitoneally. In vitro test with the aqueous extract of the plant did not show any anti-hyaluronidase activity.

Summary

1. Pharmacognostic characters of the plant, Polymnia uvedalia are described, with respect to macroscopical, microscopical, microchemical and microanalytical observations.

2. Studies on organogenesis are described with a report on the phenomenon of apomixis in this plant.

3. Preliminary chemical investigations showed that the roots contain reducing sugars, tannin and resin as the chief constituents.

4. Preliminary pharmacological investigations decribe the action of the alcoholic extract of the root on hyaluronidase and indicate the possibility of its further investigation as an antirheumatic drug.

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THE ROLE OF CHEMICAL DISINFECTION IN HOSPITALS*

By Emil G. Klarmann, Sc. D.**

Introduction

THERE is no doubt that the correct use of disinfectant products and procedures in hospitals is of great importance for the safety of everybody involved in hospital practice which means the patient, the physician, the nurse and all other personnel. One should think that the realization of this fact would impose a special kind of responsibility upon the several individuals concerned in this picture. Thus, the manufacturer or supplier of the disinfectant might be expected to have available and to supply full information as to the capacity of his product for antimicrobial action as well as to its limitations, while the doctor and nurse should be capable of selecting the particular antibacterial agents for the several purposes of hospital procedure which would offer the greatest assurance of proper performance under the conditions under which such products would be applied.

It seems unlikely that anybody would quarrel with the fundamental proposition that the usual methods of competitive business activity as observed in the general market should not apply to drugs or to any other materials whose application has a bearing upon human health or the struggle against disease. In this area, therefore, the acceptance of any such material by the medical and nursing professions should be sought not on the basis of imaginative claims, but on that of applicable and verifiable evidence.

And yet, although a very high degree of standardization has been achieved with respect to the various hospital procedures, there seems to exist considerable uncertainty with regard to the subject of disinfection of the hospital premises, as well as of specific objects used in the different departments. There is no implication in this statement that this is the fault of the administrative, the medical, the

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nursing or the housekeeping staffs of the hospitals. Rather, I think, that it is due primarily to the multitude of available antimicrobial products whose claims for effectiveness often are well ahead of their verification as to relevance to particular usage in the hospital; another factor is that scientific information concerning new products or processes is published often in technical journals, and that such information does not come early enough and in applicable form to the attention of the several echelons of hospital staffs who, by their very position and qualification, would be logically equipped to apply it practically and correctly.

Essentially, disinfection in its various aspects is a preventive procedure. To the extent that its performance involves the use of a chemical agent, it is the responsibility of the manufacturer or supplier of such an agent to make sure that his product will satisfy this preventive function fully and unequivocally.

Unlike in the case of certain anti-infective drugs designed for internal administration and possessed of a specific antimicrobial potency, i.e., of a potency directed against one or more specific microorganisms, I would deem it a fundamental requirement of a product described as a "hospital disinfectant" that it be non-specific in action, in other words, capable of killing all those microbes of epidemiological or surgical significance whose elimination is essential in the several individual phases of pertinent hospital practice. To express it differently, I believe that, when a doctor or a nurse uses a product designated as a "hospital disinfectant", they should be entirely justified in assuming that the product is capable of killing all types of disease microbes and not just some types to the exclusion of others, for example, typhoid bacilli but not staphylococci, or streptococci but not tubercle bacilli. Conversely, where there exists a problem of controlling environmental or instrument-borne infection originating with a particular microorganism, e.g., the tubercle bacillus on a TB hospital ward or in a TB sanatorium, the user of the "hospital disinfectant" should not have any reason to question whether it will or will not kill the infective organism which is of primary significance in this special case.

These remarks on the subject of required non-specificity of disinfectants are, by no means, academic since it is well-known that there exist products on the market labelled "disinfectants" to which the attribute "non-specific" cannot be applied with full propriety.

Consider, for example, the case of pine oil disinfectants. This popular type of product is notoriously weak with respect to staphylococci which it does not kill as a rule in any of the recommended use-dilutions, or even in comparatively high concentrations. Obviously, the use of such a pine oil preparation would not be indicated in an operating room where the clean-up procedure following an operation must provide for the elimination of staphylococci from the environment as a means of guarding against the risk of surgical wound infection at some later point. Similarly, there is sufficient evidence showing that quaternary ammonium compounds cannot be relied upon for tuberculocidal action. They would not, therefore, be the antibacterial agents of choice to use on premises occupied by tubercular patients since they would not offer the promise of yielding the kind of environmental control of infection, e.g., from expectorated and dried sputum particles, which one would demand of a disinfectant used under these conditions; nor would a quaternary ammonium compound lend itself satisfactorily for the disinfection of oral thermometers used either by established TB cases or even by other patients who have entered a hospital for some stated reason not connected with tuberculosis, yet may have been found subsequently to be originally unsuspected TB cases. Again, it should be emphasized that none of these examples is to be regarded as academic in character.

Definition of Terms

Up to this point, I have used only the term "disinfectant". May I now define this term, as well as certain others related to the subject of our discussion.

The designation "disinfectant" refers usually to a chemical agent which destroys pathogenic microorganisms, but not ordinarily bacterial spores; this term is used commonly of substances which are applied to inanimate objects although it is sometimes used, not quite correctly, in certain combined terms such as "skin disinfectant".

The term "antiseptic" meant originally a substance opposing sepsis by preventing or arresting the growth or action of microorganisms. Nowadays, it is used especially of agents applied to living tissue. More recently, the term "antiseptic" has acquired a precise legal connotation since it is referred to specifically in the Federal Food, Drug and Cosmetic Act as meaning the same as a "germi-

cide", except where its use involves prolonged contact with the body (as, e.g., in the case of a wet dressing, an ointment, a dusting powder, etc.), as opposed to a temporary contact (as, e.g., in the case of a mouthwash, a vaginal douche, an eye bath, etc.).

All terms construed with the suffix "-cide" imply capacity of killing; this would be true of terms such as "bactericide", "microbicide", "fungicide", "virucide", "sporicide", also of the more specific terms such as "tuberculocide".

Another suffix "-static" is used frequently to describe a capacity for prevention of microbial growth, i.e., without killing the microorganism. This suffix may be employed in general terms such as "bacteriostatic" or "fungistatic", or in more specific terms such as "tuberculostatic".

It was pointed out, in the case of the disinfectants, that they do not commonly kill resistant bacterial spores. Where sporicidal action is essential, one employs a "sterilizing" agent or process. "Sterilization", either by physical or by chemical means, is presumed to destroy all forms of life including spores and, incidentally, viruses. By the same token, the term "sterile" acquires a sharply delineated meaning as it signifies freedom from the presence of any and all forms of living matter.

A term which has come into use in the recent past is "degermation". It is intended to describe the reduction of the so-called resident bacterial skin flora by the action of certain antibacterial agents usually incorporated in soaps or detergents. "Degermation" is not synonymous with disinfection since, actually, the skin cannot be disinfected, i.e., freed from all of the bacteria present upon it.

Possibilities of Environmental Infection and Cross-Infection

Let us now review briefly the several different sources and modes of infection (and cross-infection) which are subject to control, at least in part, by suitable disinfectant procedures, as applied to the premises, the furniture, the equipment, etc. Generally speaking, one might consider the following three major possibilities:

1) contact infection,

2) droplet infection,

3) dust- and lint-borne infection.

As to contact infection, it is known that the hands of certain patients may carry infective matter acquired by contamination with their own infectious discharges, secretions, etc., and that such contamination may be transferred to the various articles handled by these patients whence it is communicated to other patients, as well as to the hospital personnel coming in contact with them.

Under the general heading of contact infection, one might refer to the following specific examples: Enteric microorganisms such as those of typhoid fever or dysentery could be disseminated by means of rectal and oral thermometers, bedpans, cystoscopes, emesis basins, etc. Pyogenic microorganisms such as streptococci or staphylococci could be transferred by surgical instruments, thermometers, bronchoscopes, etc., while respiratory pathogens such as streptococci, pneumococci, tubercle bacilli and others could be transported by thermometers, tongue depressors, broncho- and esophagoscopes, nasal instruments, etc. Pathogenic skin fungi could be deposited by carriers on floors, bath mats, bathtubs, as well as on instruments, appliances and objects of general use.

As to the second mode of the spread of infection mentioned, viz., droplet infection, it is known that forced respiratory action such as coughing or sneezing furnishes a most effective means of dispersal of infective particles, although even simple speaking may cause their projection into the environmental air for several feet. Such sputum and mucus particles may carry pneumococci, streptococci, diphtheria and tubercle bacilli in addition to other pathogens. It has been demonstrated rather convincingly that most of these droplets sediment within a rather short period of time on floors, on blankets, on furniture, etc., retaining their infectious potential often for substantial periods of time. Only a comparatively minor proportion of the expelled droplets are small enough to dry out in the air, i.e., before settling on a surface; they may remain in suspension for a long time carrying pathogens as the so-called "droplet nuclei".

The third mode of infection, viz., the dust- and lint-borne variety, is actually derived from the second. The infection-laden, sedimented, dried mucus and sputum particles are subject to redispersal into the environmental air, particularly if aided by natural drafts, by sweeping, by bed making or by some other activity in the patient's proximity. There exists satisfactory experimental evidence showing that the bacterial counts of the air are high under one or more of the con-

ditions mentioned, and low when activity is at its minimum as, e.g., in the middle of the night.

Criteria of Disinfectant Performance: Phenol Coefficient

How is the user of a "hospital disinfectant" to know that a particular product would actually furnish the kind of performance demanded under the circumstances?

Ever since disinfectants have come into general use, a long series of methods have been proposed for their evaluation. Many of these methods have been discarded, some have been retained in modified form. It is not the purpose of this paper to give a historical review of these testing methods. However, I would like to deal with some which are in use today, and which enjoy a measure of sanction, official or otherwise.

Many of you must have noticed on the labels of some of the disinfectants a legend: "phenol coefficient", with a figure after it such as 5, 6, 10, etc.

What is this phenol coefficient? Unless otherwise qualified, it is a figure indicating how many times more effective a given disinfectant is than phenol (or pure carbolic acid) against the test organism, *Salmonella typhosa,* the causative organism of typhoid fever; to obtain this information the test must be carried out under rigidly specified conditions of temperature, duration of exposure, resistance of the bacterial strain employed, and others.

It was thought, at one time, that this phenol coefficient could be regarded as a yardstick of a given disinfectant's germicidal potency, and this on the premise that the action upon the typhoid test organism paralleled that upon other pathogenic bacteria. Unfortunately, this utterly mistaken idea is still encountered in many quarters although it has been known for a long time that the assumption of any such antibacterial parallelism is devoid of general validity.

For the sake of record, it should be added, at this point, that the phenol coefficient is used as a guide for the preparation of solutions for general disinfecting purposes. The pertinent requirements which, incidentally, are enforced by a regulatory agency of the U. S. Government (viz., the Department of Agriculture) specify that such solutions must correspond in their disinfectant efficacy to a 5% carbolic acid solution. A simple mathematical computation shows that multiplying the phenol coefficient by twenty yields the dilution in which

a particular disinfectant should be employed. Thus, a product with a phenol coefficient of 5 would be employed in a dilution of 1:100 or 1%, a disinfectant with a phenol coefficient of 10 may be diluted to the extent of 1:200 or ½%, and so forth.

With specific reference to hospital disinfection, it should be noted, however, that this procedure is entirely fallacious in that it will not insure a bactericidal action upon other pathogens, comparable to that upon the test organism, *Salmonella typhosa*, and, specifically, not upon bacteria whose control by means of disinfection is essential in certain phases of hospital practice.

It was mentioned before that pine oil disinfectants are not effective against staphylococci. Thus, if a pine oil disinfectant with a declared phenol coefficient of 5 is diluted according to the formula "twenty times the phenol coefficient", the resulting solution of one part of disinfectant in one hundred parts of water would be found incapable of killing staphylococci. Actually, even when used full strength, a pine oil disinfectant may not always produce such an effect.

In the introductory comment on definitions, I touched briefly upon the term "bacteriostatic", meaning inhibitory of bacterial multiplication, but without true killing action.

This bacteriostatic effect is of great significance in connection with the testing of disinfectants; yet it is frequently overlooked, with the result that incorrect information is obtained as to the bactericidal potency of a particular product under test.

I am dwelling upon this matter at some length, for this reason: the official phenol coefficient testing method depends upon demonstration of either survival or death of the test bacteria following exposure to the action of a disinfectant when such bacteria, or rather a small portion of them, is removed and placed into a test-tube containing fresh bacteriological medium presumed to be capable of supporting bacterial multiplication. Those bacterial cells which survive the action of the disinfectant will multiply upon incubation, indicating that the particular dilution was inadequate to produce true disinfection; however, if no multiplication in the so-called subculture tube takes place, the dilution is assumed to be bactericidal.

Whether or not this procedure is sufficiently similar to what one might encounter in practice is a moot question; the fundamental problem is not whether following exposure to the action of a disinfectant there are any bacterial cells left which will multiply in the bacteriologist's glassware, but whether bacterial cells which have

been exposed to the process of disinfection under one or the other actual condition of their occurrence would become, through multiplication, a source of potential harm if subsequently they should find their way into a surgical wound or onto a susceptible mucous membrane, etc.

I am aware that, in saying this, I am introducing a factor of uncertainty with respect to bacterial death. And yet, one must not forget that a testing method, unless employed rationally, may give confusing results in that, under a particular set of experimental conditions, the microorganisms, following exposure to a given disinfectant, may appear to be dead, while the same microorganisms, when placed under favorable conditions of practical relevance, may be revealed not to be dead at all, but to remain capable of prolifieration and of causing, e.g., a generalized infection.

In this connection, one might point, as an example, to one or another preparation from the group of organic or inorganic mercurials which are known to be considerably more bacteriostatic than they are bactericidal; here, the apparent bacterial "death" as produced by a given mercurial can be reversed to "life" following contact with natural tissue fluids such as serum or blood (also with some chemicals resembling the tissue fluids in certain essential regards).

Another factor which is most significant in the evaluation of a hospital disinfectant is that of the impairing action of what is broadly referred to as "organic matter". You are aware, of course, that under practical conditions, a disinfectant is hardly ever called upon to kill bacteria in pure culture. Actually, such pathogens occur in association with various forms of organic matter, e.g., urine, pus, mucus, etc.

It is noteworthy, therefore, that some disinfectants are so indiscriminately reactive with extraneous material of this type that much, if not most, of their antibacterial potential is dissipated by interaction with it, leaving little if any for the attack upon bacteria whose elimination is being aimed at by disinfection. This observation applies to different classes of disinfectants, and especially to those based upon halogens, such as the hypochlorites, which should be applied logically only to those surfaces or objects whose load of organic matter has been reduced substantially by prior cleaning.

There is much more that could be said concerning the rather limited character of the information supplied by a disinfectant's phenol

coefficient. I believe that the few examples given will suffice for illustrative purposes.

The "Use-Dilution Confirmation" Test

More recently, the agency of the U. S. Government to which I referred before as being in supervisory charge of regulating the handling of disinfectants, has taken cognizance of the potentially misleading character of this phenol coefficient information. As a result, a new testing procedure has been set up which, among other things, attempts to protect the hospital user of disinfectants against products of questionable value to hospitals.

This new procedure, known as the "Use-Dilution Confirmation Test", requires that a particular disinfectant dilution, recommended for use upon hospital premises, must be capable of killing a representative enteric microorganism (*Salmonella choleraesuis*), as well as a representative pyogenic microorganism (*M. pyogenes* var. *aureus*), when deposited on a solid surface. In providing for a well-defined set of experimental conditions under which the test must be carried out, it endeavors to simulate practical disinfectant usage.

With the aid of this test, a number of significant findings have been obtained, some of which are of interest with reference to our subject.

As to the pine oil disinfectants, it has been confirmed by the new test method that, indeed, they are not suited for hospital disinfection because they are not capable of killing staphylococci in any practical use-dilutions.

With respect to coal tar disinfectants, those of the so-called "emulsifiable" variety (which form milky emulsions when diluted with water) as a rule yield use-dilutions (as derived from their respective phenol coefficients) which may be several times weaker than required to assure germicidal action upon staphylococci. No such wide discrepancy is encountered in the case of the so-called "soluble" variety (forming clear solutions with water) whose use-dilutions as derived from their phenol coefficients approximate those found to be effective under the conditions of the new testing technique.

Marked discrepancy between the phenol coefficient derived use-dilutions and those required to kill both the salmonellae and staphylococci in the new test has been found in the case of quaternary

ammonium compounds. Here, often considerably higher concentrations than those recommended right along appear to be necessary for a reliable job of disinfection.

While all this material is a matter of published record and, indeed, might have been used in a program of instruction to hospitals by the government authority mentioned, it is an unfortunate fact that, for one reason or another, such information does not reach those who would be most vitally interested in it. The sad result is that the practice of using either incorrect types of disinfectants, or solutions which are too weak for the desired effectiveness, is quite prevalent in many hospitals.

Only brief mention can be made here of yet another factor deemed to be significant, viz., that of the persistence of the antibacterial potential on disinfected surfaces.

With reference to the disinfection of hospital premises, it is evident that the usual methods of evaluation of disinfectants do not supply information on one important question, viz., how long the effect of disinfection will last. An answer to this question should be available, however, as it will determine the frequency with which disinfection should be practiced to insure a continuity of the antibacterial potential of disinfected surfaces and objects. Extensive studies have shown that some disinfectants are fugitive in action, while the effect of others may endure for days or weeks after application. Other things being equal, it is obvious that preference should be given to products of the latter category since they not only eliminate microbial contamination at the moment of application, but continue to exert antimicrobial action upon pathogens falling upon the disinfected surface for some time after the application of the disinfectant.

Special Utility Disinfectants (for Instruments, etc.)

In addition to the general types of disinfectants, i.e., those for use on hospital premises with the view to reducing the risk of environmental infection and cross-infection, there are several groups of disinfectants serving special purposes; the most important, from the hospital point of view, is the group of instrument disinfectants.

Many instruments used in operative procedure are subjected to sterilization in autoclaves where steam under pressure produces the

desired effect. Properly performed autoclaving may be regarded as sterilization in the true sense of the word, i.e., elimination of all living matter in the form of bacteria, bacterial spores or viruses. If you refer to the definition of the term "disinfectant" you will remember that this definition does not cover sporicidal action. Incidentally, when speaking of "sporicidal" action, I mean the action upon the *resistant* bacterial spores such as those of the bacilli associated with gas gangrene or with lockjaw. I am saying this because there are spore-forming bacteria whose spores are less resistant to the action of disinfectants than those mentioned; and still less resistant are the spores of pathogenic fungi.

Of all of the form of microbial life, the resistant bacterial spores are those most difficult to kill by chemical disinfectants acting at room temperature. Of course, they can be killed by corrosive chemicals; but such chemicals would also attack the objects upon which these spores might occur.

Fortunately, the problem of destruction of bacterial spores is not usually of routine importance. Admittedly, there are cases where such spores must be eliminated and where, therefore, measures must be taken to insure a sporicidal effect. If, for some reason, autoclaving, as a sporicidal procedure, cannot be resorted to, only those chemical disinfectants should be employed for which a sporicidal action is definitely being claimed by a reliable manufacturer. In this connection, it must be remembered that compared with bactericidal action the sporicidal action of chemical disinfectants is very much slower. Actually, there is sufficient evidence to suggest that an exposure period of less than 24 hours may not be adequate in that it may not yield uniformly sporicidal results. In any case, one should not be misled by a claim to the effect that a particular disinfectant kills "spore-formers" or "spore-forming bacteria". A spore-former usually represents the vegetative stage of a germ capable of producing spores; the resistance to the action of disinfectants of this vegetative form is not any greater than that of other strictly vegetative bacteria which are not capable of producing spores. Thus, the claim for a capacity to kill "spore-formers" need not, and usually does not, imply a capacity for killing the spores themselves.

Two important factors to be considered in connection with the chemical sterilization of surgical instruments are the type of instrument to be sterilized and the extent of its contamination. As to the

former, it is obvious that if the instrument is substantially smooth, without any ridges or crevices, its contamination can be dealt with more readily than if it has some protected surfaces, hinges, etc. As to the latter, it must be clear that the contaminating load may determine the success or failure of chemical sterilization, particularly in the case of formaldehyde solutions, since formaldehyde is one of those reactive chemicals whose antibacterial action may be reduced appreciably in the presence of any significant amounts of organic matter. All this suggests the desirability of prior mechanical cleansing of the instruments; without such cleansing there is the additional risk that coagulation of albuminous matter coating the used instrument may cause entrapment of large numbers of bacteria in the coagulum which may render the adequacy of the treatment of the instrument decidedly questionable.

Where heat can be used, but autoclaving is not available, boiling water is sometimes resorted to as a means of effecting sporicidal action. It should be noted, however, that resistant spores may require boiling for several hours before they are killed. It may be helpful to know, therefore, that the addition of small portions of certain nonvolatile phenolic disinfectants to boiling water (of the order of 2 to 3%) will produce a sporicidal effect with respect to resistant bacterial spores (such as those of *Clostridium sporogenes* or *Clostridium tetani*) in as little as ten minutes. The advantage of this procedure is immediately evident if one remembers not only the great convenience of a shortened boiling time, but also the fact that the deleterious action of boiling water on metal, in terms of rusting or dulling of sharps, is thereby greatly minimized. Incidentally, this procedure should be applicable to the sterilization of needles and syringes since simple immersion in a chemical solution may cause formation of an air pocket which would prevent the contact of the area with the chemical.

When reviewing the disinfection of hospital premises, I emphasized the need of insuring tuberculocidal action. While there is a debate going on as to whether or not the broad term "disinfectant" implies a capacity of killing tubercle bacilli in the process of disinfection, there can be no valid objection to the proposition that a "hospital disinfectant" ought to be possessed of demonstrable tuberculocidal action. I believe that the validity of this proposition should extend to instrument disinfectants and, particularly, to those which are used to disinfect instruments with optical systems and which cannot stand

heat treatment. Obviously, the chemicals employed should not have any damaging effect either, e.g., upon the cement mountings or the optical parts of such objects. Clinical thermometers belong in the same category since they cannot be heat sterilized, yet represent potential vectors of a multitude of pathogens, including tubercle bacilli. This is why their disinfection must assure tuberculocidal action especially in the presence of sputum. Although alcohol has been credited for some time with a capacity for satisfactory disinfection of oral thermometers, some recent data cast serious doubt upon its claimed antitubercular efficiency. On the other hand, certain synthetic phenolic disinfectants have been giving satisfactory results when used for the routine disinfection of thermometers.

The Problem of Virucides

Now what about virucidal action? If we accept the modern idea as to the nature of a virus, we should characterize it as a form of nucleoprotein which, unlike a bacterium, cannot multiply directly, but requires a suitable host whose structural material it utilizes for the elaboration of its own type of nucleoprotein.

There are many different types of proteins with special characteristics often developed to an extremely sensitive degree. These proteins can be deprived of their natural status, i.e., denatured, by a variety of means which differ widely with the individual types of the proteins. Such denaturation can be effected by heat or by the action of different chemicals. Often, a slight change in the reaction, i.e., a shift from acid to alkaline or vice versa will suffice. A somewhat similar situation exists in the case of the virus nucleoproteins. All of them can be inactivated by heat; some of them respond to the inactivating action of one kind of chemical, some to another. Thus, influenza virus is inactivated by several different kinds of chemicals. Of course, one has heard enough about the Salk polio vaccine to know that the poliomyelitis virus is inactivated by formaldehyde. You will please note that, in connection with viruses, I prefer not to use the expression "killing", but rather "inactivation" because viruses are not living entities in the strict sense of the word.

However, there is a factor to be kept in mind here which to some extent corresponds to a factor in the disinfection directed against bacteria, and that is the effect of organic matter. Here, too, a disinfectant which is highly reactive such as a halogen or an oxidizing

agent may produce inactivation of the virus protein if this virus protein is present in a reasonably pure or in a diluted form, or both. On the other hand, where the virus occurs in the presence of a substantial quantity of organic matter of one sort or another (which is the practical condition demanding disinfection), the chemical disinfectant may dissipate its inactivating energy to a very marked degree by reacting with the constituents of the organic matter rather than with the virus protein. This is why I believe that claims for virucidal action in general, or for poliocidal action in particular, as advanced occasionally on behalf of some disinfectants should be accepted with caution. They may be based upon laboratory tests performed with purified or with diluted virus cultures, but they need not necessarily assure virucidal performance under the conditions of practical disinfecting procedure.

Some of you may have been faced with the problem of another virus infection, viz., that of infectious hepatitis. The opinion has been expressed that this disease can be spread, among other things, by infected syringes and needles. At this time, it is not known whether any chemical disinfectant acting at room temperature can inactivate this hepatitis virus under the practical conditions of its occurrence. The reason is that, as of now, hepatitis virus can propagate only in humans; since, therefore, animal experimentation is not feasible, one could work only with human volunteers, and this is something which is not exactly simple to arrange as you may well imagine. Here is another reason for suggesting with some emphasis that syringes and needles be sterilized either by autoclaving or by boiling in a diluted solution of a non-volatile phenolic disinfectant.

Desirable Properties of a General Utility Disinfectant

At this point, you might be justified in asking me what I would consider to be a satisfactory disinfectant for hospital use. Of course, if you followed me up to this point, you might conceivably draw your own conclusions with reference to a number of several specific applications in the hospital area.

I have been endeavoring to indicate not only what chemical disinfectants might be expected to accomplish, but also what they cannot be expected to do. And so, to answer the question, let us again review the summary information under two general headings.

When considering a general utility hospital disinfectant, in other words one intended for environmental disinfection (as a means of

controlling direct as well as cross-infection), I would say that such a disinfectant should satisfy the following requirements:

1) It should be completely non-specific, i.e., germicidal for all pathogenic microorganisms of possible significance in the hospital picture. This germicidal action must be rapid and true, i.e., irreversible rather than inhibitory.

2) In view of the ubiquitous occurrence of "organic matter" in its various forms under practical conditions, the disinfectant should not suffer so marked a reduction of its bactericidal potency in the presence of organic matter which would render a reliable germicidal performance questionable.

3) Since infective material is being disseminated continually, the disinfectant should have a persistent rather than a fugitive action so as to assure the retention upon the disinfected surface or object of an antimicrobial potential for some time and logically, between successive applications of the disinfectant.

The above three requirements apply to the performance. In addition, I would like to submit, for your consideration, the following supplementary requirements:

4) The disinfectant should be safe in use. It should not be poisonous nor damaging to the human skin.

5) It should not affect the materials with which it comes in contact by corroding, staining or other deleterious action.

6) When diluted for use, it should not emit any obnoxious, persistent odor which, as is known, may have an objectionable psychological effect on both patients and personel.

Qualifications of an Instrument Germicide

Under the heading of chemical disinfectants for instruments I would have this to say.

One must proceed with the premise that, while many operating room instruments, appliances, etc., permit sterilization by autoclaving, some cannot be autoclaved. (Incidentally, clinical thermometers also belong in the latter category.)

Where chemical disinfection is applied, the solution should be rapidly active, and should evidence the broadest possible non-specific

microbicidal efficiency; the latter should include, particularly, a demonstrable capacity for tuberculocidal action. The presence of organic matter should not cause inactivation or substantial reduction of its antimicrobial potency.

Where sporicidal action is deemed essential but cannot be achieved by autoclaving (because a particular instrument would not tolerate such treatment), the instructions regarding the use of a sporicidal, chemical disinfectant should be reliable as well as specific as to precleaning of the instrument, concentration of the disinfectant to be used, and duration of exposure. This information should be derived from experience with the most resistant bacterial spores of logical relevance to hospital procedure and should be utilized so as to embody a safety factor of adequate magnitude.

Where sporicidal action is demanded but autoclaving is not available or is impractical, a suitable chemical disinfectant should be added to boiling water so as to render the performance of the solution reliably sporicidal in a short time.

Of course, the disinfectant should not damage surgical instruments and appliances, nor injure human skin, when used as directed.

Concluding Remarks

The selection of a chemical disinfectant for use in hospitals should not be treated as an unimportant or inconsequential matter. I believe to have proved to you that the likelihood of infection and cross-infection in hospitals, by one or more of the several possible routes, depends upon the rational selection and correct application of disinfectants. In this picture, the responsibility of the informed manufacturer or supplier plays an important role inasmuch as it is he who should furnish to the hospital staff information not only regarding the advantages of his product, but also regarding its limitations. However, in the last analysis, it is up to the different members of the hospital staff who are charged with the performance of the respective services aiming at the prevention of infection to make sure that the antimicrobial agents handled by them will satisfy their intended mission effectively and dependably. Correct disinfection may mean the difference between health and sickness, or even between life and death.

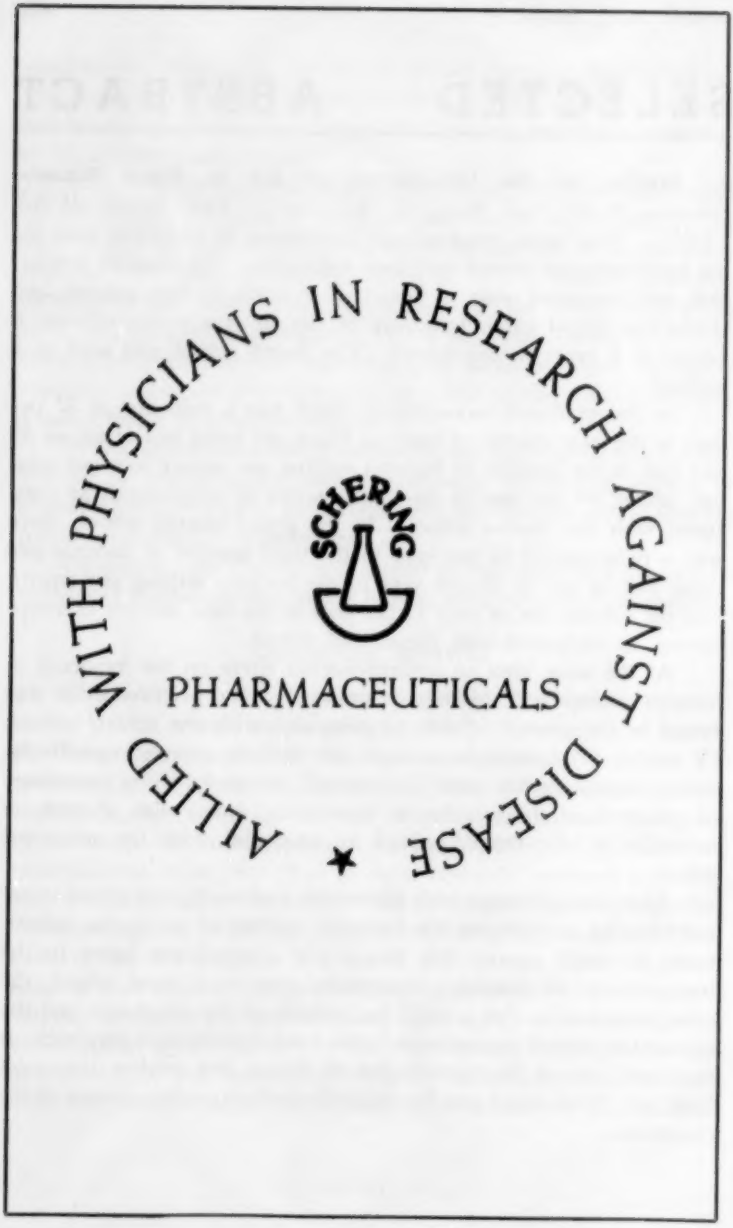
SELECTED ABSTRACT

Studies on the Disinfection of Air in Rural Schools. Gilcreas, F. W., and Read, H. R. *Am. J. Pub. Health 45:767* (1955). Four large rural schools cooperated in providing data for the bacteriological studies and their evaluation. Ultra-violet irradiation was evaluated over a period of 9 years in two schools and triethylene glycol vapor treatment of the air was evaluated over a period of 6 years in one school. The fourth school was used as a control.

In the irradiated rooms tested, there was a reduction of 37 per cent in the total number of bacteria found per cubic foot of air, of 39 per cent in the number of bacteria settling per square foot per minute, and of 44 per cent in the total number of streptococci, as compared with the control school. In the glycol treated school, there was a reduction of 60 per cent in the total number of bacteria per cubic foot of air, of 55 per cent in the bacteria settling per square foot per minute, but of only 11 per cent in the total number of streptococci, as compared with the control school.

At the same time an epidemiological study on the incidence of measles, mumps and chickenpox was carried out. No reduction was found in the treated schools as compared with the control school. Of course, since these diseases are all viral, no correlation with the bacteriological studies could be expected. A study of the percentage of person-days absence due to respiratory illness also showed no reduction in the treated school as compared with the untreated school.

Therefore, although both ultraviolet and triethylene glycol vapor are effective in reducing the bacterial content of air in the schoolroom, it would appear that this is not a significant factor in the transmittance of disease. Apparently, even in a rural school, the other associations that a child has outside of the classroom and the chance for contact transmission in his total environment play such an important role in the transmission of disease that neither ultraviolet light nor glycol vapor can function effectively to reduce illness in the classroom.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